



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------------------------|-----------------------------|
| 10/594,419 | 05/22/2007 | Stefan Theis | DEAV2004/0025 US PCT | 8067 |
| 5487 | 7590 | 11/16/2009 | | |
| ANDREA Q. RYAN SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807 | | | EXAMINER HIRIYANNA, KELAGINAMANE T | |
| | | | ART UNIT 1633 | PAPER NUMBER |
| | | | NOTIFICATION DATE 11/16/2009 | DELIVERY MODE ELECTRONIC |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPatent.E-Filing@sanofi-aventis.com
andrea.ryan@sanofi-aventis.com

Office Action Summary

Application No.

10/594,419

Applicant(s)

THEIS ET AL.

Examiner

KELAGINAMANE T. HIRIYANNA

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 4-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2 and 4-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/CDC)
- Paper No(s)/Mail Date 05/22/2007.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Applicant's response filed on 10/01/2009 in response to office action mailed on 09/30/2009 has been acknowledged.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

Restriction of invention

Applicant's election without traverse of restriction requirement in the reply filed on August 22, 2008 is acknowledged. Applicant elects without traverse the invention Group I (Claims 1-2, 4-9) for further prosecution on merits.

Claims 1-2 and 4-9 are pending and presently under examination.

Claims 10-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected claims, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 10/01/2009. Further placing of claims 27-28 and 30-35 in a separate (unelected) Group V is made final upon on Applicants approval..

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2 and 4 are rejected under 35 U.S.C. 101 because claim is drawn to non-statutory subject matter as follows:

Claims 1-2 and 4 as written do not sufficiently distinguish host cell as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory

subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated " or "recombinant" before "mammalian cell" (non-human; see below). See MPEP 2105.

Claims 5 is similarly rejected because immortalization can occur in the absence of the hand of man, e.g., cancers.

Claims 6-9 are rejected because of they depend from rejected claims.

Claims 6-8 are drawn to a recombinant mammalian cell. When read broadly this encompasses live human beings as genetically engineered. It is PTO policy not to allow claims to humans (1077 O.G. 24 April 1987). The insertion of a phrase such as 'an isolated mammalian cell', or "a non-human mammalian cell" or 'excluding the human organism' would overcome this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 and 4 are rejected under 102(b) as being anticipated by Diaz et al., (2000, Cytotechnology 34:22-236).

The above claims are drawn to a mammalian cell having first and second side forming the outer surface of the cell and which first and second sides are distinguished from each other by localization on first side a functional hNTCP protein and second side carries a functional HBSEP protein.

Diaz teaches a mammalian and human hepatocyte that is polarized having at least two sides namely basolateral (sinusoidal) membrane and Canalicular (apical membrane) wherein basolateral membrane functional NTCP protein is localized and on the canalicular side functional BSEP protein is localized (entire article; abstract; p.227, Figure 1; p.227 col.1-2; p.231, col.2, 2nd paragraph bridging p. 232). Thus the rejected claims are within the scope of the Diaz's disclosure.

Claims 1-2 and 4-9 are rejected under 102(b) as being anticipated by Kagawa et al., (2003, Hepatology 38:389A; art of record).

The above claims are drawn to a mammalian cell having first and second side forming the outer surface of the cell and which first and second sides are distinguished from each other by localization on first side a functional hNTCP protein and second side carries a functional hBSEP protein.

Kagawa clearly teaches recombinant constructs expressing NTCP and BSEP in MDCKII cells and the functional expression of said proteins in said cells and concludes that this novel system permits simultaneous analysis of Bsep functionm distribution, regulation etc (Abstract). Thus the rejected claims are within the scope of Kagawa's disclosure.

Claims 1-2 and 4 are rejected under 102(b) as being anticipated by Choudhuri et al., (2003, Drug Metabolism and Disposition).

The above claims are drawn to a mammalian cell having first and second side forming the outer surface of the cell and which first and second sides are distinguished from each other by localization on first side a functional hNTCP protein and second side carries a functional hBSEP protein.

Choudhuri teaches a mammalian tissue cells of choroid plexus, liver, kidney and ileum and teaches the cells especially the liver cells that are known in the art to be polarized as having expression of NTCP and BSEP (entire article; abstract; p.1343, Figure 7) and it is inherent that these proteins is localized on different sides on the cell

membrane because these cells are polarized. Thus the rejected claims are within the scope of the Choudhuri's disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-2 and 4-9 are rejected under 35 USC 103 (a) as being unpatentable over Diaz et al., (2000, Cytotechnology 34:22-236) and Kagawa et al., (2003, Hepatology 38:389A; art of record) in view of Kullak-Ublick. et al (2000, Cytotechnology 34:1-9) and Cui et al (2001, Molecular Pharmacoecology 60:934-943; art of record).

The above claims are drawn to a mammalian cell having first and second side forming the outer surface of the cell and which first and second sides are distinguished from each other by localization on first side a functional hNTCP protein and second side carries a functional hBSEP protein.

Diaz teaches a mammalian and human hepatocyte that is polarized having at least two sides namely basolateral (sinusoidal) membrane and Canalicular (apical membrane) wherein basolateral membrane functional NTCP protein is localized and on the canalicular side functional BSEP protein is localized (entire article; abstract; p.227, Figure 1; p.227 col.1-2; p.231, col.2, 2nd paragraph bridging p. 232). Diaz however, does not teach recombinant cells with vectors expressing functional hNTCP or hBSEP.

Kagawa clearly teaches recombinant constructs expressing NTCP and BSEP in MDCKII cells and the functional expression of said proteins in said cells and concludes that this novel system permits simultaneous analysis of Bsep functionm distribution, regulation etc (Abstract).

Kullak-Ublick clearly teaches expressing recombinant NTCP functional protein expression. in human hepatoblastoma HepG2cells as Ntcp-GFP fusion protein (entire article; abstract; p.7 bridging p.8). Kullak-Ublick further teaches that the fusion protein

follows the same sorting route and functionally identical to naturally occurring NTCP protein (entire article; abstract).

Cui clearly teaches double transfected MDCK cells functionally expressing a human transporter SLC21A8 that is closely related to NTCP/SLC10A1 and ABCG2 that is closely related to BSEP/ABCB11) and concludes that the double transfected cells provide a useful system for the identification of transport substrates and transport inhibitors including drug candidates.

Thus it would have been obvious for one of ordinary skill in the art to incorporate into polarized cells of Diaz the expression of recombinant functional NTCP expression as taught by Kagawa and/or Kullak-Ublick and the expression of functional recombinant BSEP expression as taught by Noe et al and use the double transfected cells provide a useful system for the identification of transport substrates and transport inhibitors including drug candidates as indicated by Cui. One of ordinary skill in the art would have reasonable expectation of success making using polarized cell expressing both NTCP and BSEP as the art clearly teaches that it is routine to clone and express heterologous gene or cDNA in a mammalian cell and art further clearly teaches that polarized cells are equally amenable to such manipulation and useful. Thus, the claimed invention was *prima facie* obvious.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.*, whose telephone number is (571) 272-3307. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system,

Art Unit: 1633

contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633